

REMARKS

Status of the Claims

Claims 125-132 and 148-149 are pending in the present application. Claim 149 is new. Support for new claim 149 is found throughout the application including, for example, in claim 20 of the originally filed PCT application. No new matter is entered by way of this amendment. Reconsideration is respectfully requested.

Issues under 35 U.S.C. § 102

Claims 125-132 and 148 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Fiegler *et al.*, *Genes, Chromosomes & Cancer*, 36:361-374, ("Fiegler"), *see Office Action*, pages 2-5. Applicants respectfully traverse.

The Examiner has maintained the rejection of claims 125-132 and 148 as allegedly lacking novelty in light of Fiegler. Applicants note that the earlier novelty rejection in light of PCT Publication No. WO 00/24925 to Hussey *et al.* has been withdrawn, *see Office Action*, page 5, item 7.

In maintaining the rejection based on Fiegler, the Office Action relies on the disclosure in the section "Hybridisation to Microarrays" spanning the columns on page 364 of Fiegler. This section describes pre-hybridization of an array of amplified PCR products with Cot-I DNA. Later sections of Fiegler subsequently describe the hybridization of PCR products derived from male and female cells to the pre-hybridized array, *see, e.g.*, the section entitled "Testing of Clone Hybridisation Characteristics", column 2, page 364 of Fiegler.

The claims are novel in view of Fiegler

In light of the above, the Office Action alleges that the subject matter of claim 125 is not novel in light of Fiegler. However, Applicants submit that the Office Action mischaracterizes the instant claims and/or the disclosure of Fiegler. For example, in the present application claim 125 clearly defines that randomly amplified PCR products, which are depleted of repetitive sequences, are attached to a solid substrate. Thus, the DNA attached to the solid substrate is depleted of repetitive sequences. In contrast, the method of Fiegler attaches non-repeat depleted DNA to the substrate and then attempts to mask the repetitive sequences in the DNA on the substrate using a pre-hybridization step.

In light of the above, Applicants submit that the disclosure of Fiegler does not fall within the scope of independent claim 125. Accordingly, independent claim 125 and the claims dependent therefrom are novel in light of Fiegler. Withdrawal of the rejection is respectfully requested.

Applicants further note that the Office Action rejected claim 148, which defines the method of claim 125 using 100 or less cells with a first karyotype. It appears the Office Action has extended the novelty rejection to claim 148 without supporting the rejection of claim 148 at all, as the Office Action makes no mention of where in Fiegler the disclosure of the subject matter of claim 148 occurs.

As described above and further herein below, Applicants submit that all claims in the application are already novel and inventive over the disclosure of Fiegler. Notwithstanding, Applicants submit that Fiegler fails to disclose any Comparative Genomic Hybridization method using DNA amplified from 100 or less cells, as defined in claim 148. Thus, Applicants submit that claim 148 should also be considered novel and inventive over the disclosure of Fiegler, irrespective of the novelty of claim 125.

The claims are not obvious over Fiegler

In addition, Applicants submit that the differences between the presently claimed method and the method disclosed in Fiegler are not merely trivial differences. The advantages of the method of the present invention over the method described in Fiegler are set out below. Applicants submit that at the time of the invention, these advantages would not have been expected by an ordinary artisan from the cited reference.

- The arrays used in the method of the present invention should be more sensitive than the arrays used in the method disclosed in Fiegler. Specifically, much of the immobilized DNA in the arrays in the Fiegler method would be blocked by Cot-1 DNA during the pre-hybridization step, leaving only a fraction of the immobilized DNA available for hybridization with the test and reference DNA during the main hybridization step. In contrast, in the method of the present invention, which does not use a pre-hybridization step, substantially all of the DNA immobilized to the array would be available for hybridization during the main hybridization step.
- Elimination of the pre-hybridization step would also eliminate any user variability or error in this step, thus improving the reliability and/or reproducibility of the method

relative to the method disclosed in Fiegler.

- The pre-hybridization step used in the Fiegler method adds an additional 60 minutes time compared to the method of the present invention. As comparative genomic hybridization is commonly used for pre-implantation genetic screening where the rapidity of the assay is important, the shorter duration of the assay of the present invention represents a significant advantage over the method disclosed in Fiegler.
- The use of a pre-hybridization step in Fiegler also introduces the potential for drying of the pre-hybridization mixture on the array. Once DNA based solutions dry to an array, the array is essentially destroyed. Therefore, elimination of the pre-hybridization step would improve the reliability of the method, as the chance of array failure as a result of drying in the prehybridization step is eliminated.
- The method disclosed by Fiegler uses substantially more Cot-1 DNA than the method of the present invention. For example, the Fiegler method uses 67.5 μ g of Cot-1 DNA in the pre-hybridization step and the same amount again in the hybridization mix, for a total of 135 μ g. In contrast, the method of the present invention uses only 35 μ g in the hybridization step and no pre-hybridization step is used. As a result, Fiegler's method utilizes almost 4x the amount of Cot-1 used in the method of the present invention. As Cot-1 DNA is a substantial expense in the performance of CGH methods, the method of the present invention is significantly more economical than the method of Fiegler.

In view of the foregoing, Applicants submit that the claims are non-obvious, as well as novel, in view of Fiegler. A Notice of Allowance is respectfully requested.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

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